IN THE CLAIMS:

Please cancel Claims 1-8 and 20, and amend Claims 16, 17, and 19, all without prejudice. The specific changes to the amended claims are shown on a separate set of pages attached hereto and entitled **VERSION WITH MARKINGS TO SHOW CHANGES MADE**, which follows the signature page of this Amendment. On this set of pages, the insertions are double underlined while the ~~deletions are struck through~~. A clean version of the entire set of pending claims is attached as a separate set of pages and entitled **CLEAN VERSION OF THE ENTIRE SET OF PENDING CLAIMS.**

REMARKS

The present invention is related to a procedure to block the replication of reverse transcriptase dependent viruses by the use of inhibitors of deoxynucleotides synthesis. Claims 9-19 are being examined in this application. Claims 1-8 and 20 have been canceled as being directed to a single compound. Claims 16, 17, and 19 have been amended to give the full names for all acronyms. The claims meet the written description and "how to make" and "how to use" enablement requirements of 35 USC § 112, first paragraph, as well as the definiteness requirement of 35 USC § 112, second paragraph, per Balzarini, J., "Effect of antimetabolite drugs ..." Pharmacol Ther 2000 Aug-Sep, 87(2-3):175-187 attached. Balzarini confirms that, in view of the combination of hydroxyurea (HU), a ribonucleotide reductase inhibitor, and 2',3'-dideoxyinosine (ddI), a nucleoside reverse transcriptase inhibitor (NRTI), as disclosed in the Lori et al. patents, it was obvious that this principle should be viable for the combination of other NRTIs (page 179, second column, first line of new paragraph), such as the NRTIs clinically approved or currently subjects of clinical trials for treatment of HIV: AZT (zidovudine), ddC (zalcitabine), d4T (stavudine), 3TC (lamivudine), ABC (abacavir), and 2'-F-dd-ara-A (lodenosine) (page 176, column 1, 3rd paragraph). It was also obvious that any modality that would deplete the intracellular pool of deoxyribonucleoside phosphates could substitute for HU (page 185, column 1, 1st paragraph). As for the disclosures of the Malley et al. patents which specifically exclude the combination of HU

and AZT as inactive against HIV in quiescent cells in culture, the disclosures of the Lori et al. patents specifically include the combination of HU and AZT as active against HIV in activated cells in culture. Before preparing a terminal disclaimer to obviate a double patenting rejection over USPs 5,521,161, 5,736,527, 6,046,175, and 6,194,390, Applicant respectfully brings USP 6,093,702 to the attention of the patent office for its consideration. Reexamination and reconsideration of the application, as amended, are respectfully requested.

CONCLUSION

In view of the above, it is submitted that the claims are in condition for allowance. Reconsideration and withdrawal of all outstanding rejections are respectfully requested. Allowance of the claims at an early date is solicited. If any points remain that can be resolved by telephone, the Examiner is invited to contact the undersigned at the below-given telephone number.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 11/13/01

By: _____

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

On this set of pages, the insertions are double underlined while the ~~deletions are struck through~~.

9. (Pending) A method for inhibiting replication of reverse transcriptase dependent virus in animal cells, comprising the steps of administering to said cells a compound that depletes the intracellular pool of deoxyribonucleoside phosphate, in conjunction with administering to said cells an antiviral nucleoside phosphate analog.

10. (Pending) The method of claim 9, wherein said deoxynucleoside phosphate depleting compound is an inhibitor of ribonucleotide reductase.

11. (Pending) The method of claim 10, wherein said compound is hydroxyurea.

12. (Pending) A method for inhibiting replication of reverse transcriptase dependent viruses in animal cells, comprising the steps of administering to said cells a first compound that depletes the intracellular pool of deoxyribonucleoside phosphate, in conjunction with a second compound that serves to inhibit replication of said virus by terminating DNA chain elongation.

13. (Pending) The method claim 12, wherein said second compound inhibits replication by premature termination of viral DNA synthesis to produce incomplete viral DNA.

14. (Pending) The method of claim 12, wherein said first compound is an inhibitor of ribonucleotide reductase.

15. (Pending) The method of claim 14, wherein said first compound is hydroxyurea.

16. (Amended) The method of claim 15, wherein said second compound is selected from the group consisting of 2',3'-dideoxyinosine (ddI), 2',3'-dideoxycytidine (ddC), 2'-fluoro-2',3'-dideoxyarabinosyl adenosine (2'-F-dd-ara-A), 2'-fluoro-2',3'-dideoxyarabinosyl inosine (2'-F-dd-ara-I) and 2'-fluoro-2',3'-dideoxyarabinosyl guanosine (2'-F-dd-ara-G).

17. (Amended) The method of claim 12, wherein said second compound is selected from the group consisting of a dideoxynucleoside and 3'-azido-2',3'-dideoxythymidine (AZT).

18. (Pending) The method of claim 16, wherein said dideoxynucleoside is a 2'-fluoro purine dideoxynucleoside.

19. (Amended) The method of claim 16, wherein said dideoxynucleoside is selected from the group consisting of 2',3'-dideoxyinosine (ddI), 2',3'-dideoxycytidine (ddC), 2'-fluoro-2',3'-dideoxyarabinosyl adenosine (2'-F-dd-ara-A), 2'-fluoro-2',3'-dideoxyarabinosyl inosine (2'-F-dd-ara-I) and 2'-fluoro-2',3'-dideoxyarabinosyl guanosine (2'-F-dd-ara-G).

CLEAN VERSION OF ENTIRE SET OF PENDING CLAIMS

9. (Pending) A method for inhibiting replication of reverse transcriptase dependent virus in animal cells, comprising the steps of administering to said cells a compound that depletes the intracellular pool of deoxyribonucleoside phosphate, in conjunction with administering to said cells an antiviral nucleoside phosphate analog.

10. (Pending) The method of claim 9, wherein said deoxynucleoside phosphate depleting compound is an inhibitor of ribonucleotide reductase.

11. (Pending) The method of claim 10, wherein said compound is hydroxyurea.

12. (Pending) A method for inhibiting replication of reverse transcriptase dependent viruses in animal cells, comprising the steps of administering to said cells a first compound that depletes the intracellular pool of deoxyribonucleoside phosphate, in conjunction with a second compound that serves to inhibit replication of said virus by terminating DNA chain elongation.

13. (Pending) The method claim 12, wherein said second compound inhibits replication by premature termination of viral DNA synthesis to produce incomplete viral DNA.

14. (Pending) The method of claim 12, wherein said first compound is an inhibitor of ribonucleotide reductase.

15. (Pending) The method of claim 14, wherein said first compound is hydroxyurea.

16. (Amended) The method of claim 15, wherein said second compound is selected from the group consisting of 2',3'-dideoxyinosine (ddI), 2',3'-dideoxycytidine (ddC), 2'-fluoro-2',3'-dideoxyarabinosyl adenosine (2'-F-dd-ara-A), 2'-fluoro-2',3'-dideoxyarabinosyl inosine (2'-F-dd-ara-I) and 2'-fluoro-2',3'-dideoxyarabinosyl guanosine (2'-F-dd-ara-G).

17. (Amended) The method of claim 12, wherein said second compound is selected from the group consisting of a dideoxynucleoside and 3'-azido-2',3'-dideoxythymidine (AZT).

18. (Pending) The method of claim 16, wherein said dideoxynucleoside is a 2'-fluoro purine dideoxynucleoside.

19. (Amended) The method of claim 16, wherein said dideoxynucleoside is selected from the group consisting of 2',3'-dideoxyinosine (ddI), 2',3'-dideoxycytidine (ddC), 2'-fluoro-2',3'-dideoxyarabinosyl adenosine (2'-F-dd-ara-A), 2'-fluoro-2',3'-dideoxyarabinosyl inosine (2'-F-dd-ara-I) and 2'-fluoro-2',3'-dideoxyarabinosyl guanosine (2'-F-dd-ara-G).

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